WEST Search History

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Search Notes

DATE: Wednesday, September 27, 2006

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR	
☐	L1	peptide.ti,ab,clm. same (wy or pp or ap or py or ppy or ppf or ppw or app or wys or wyt or lwy or ggy or gpy or ppyd or ppfd or fdpp or ggyl or ppwd or slwy or pxwy or wyxxp or yxy or pwst or ekkxf or wxy or ywxy).ti,ab,clm.	750
☐	L2	l1 and (sugar or sacchcaride or polysaccharide or los or lps)	215
☐	L3	l1 and (sugar or saccharide or polysaccharide or los or lps)	224
☐	L4	los.clm. and mimotope.clm.	2
☐	L5	(anti-id or antiid or antiidiotyp$).ti,ab,clm.	208
☐	L6	L5 and neisser$	6
☐	L7	neisseria.clm. same peptide.clm.	48
☐	L8	L7 and $tope	31
☐	L9	neisser$ same mimotop$	5
☐	L10	(di-peptide or dipeptide or tri-peptide or tripeptide).clm.	1781
☐	L11	L10 and (proline or pp or glyglytyr or wys or wyt or lwy or ggy or gpy or propropro or ppp).clm.	258
☐	L12	L10 same (proline or pp or ppy or py or ppf or ppw or app or alapropro or glyglytyr or wys or wyt or lwy or ggy or gpy or propropro or ppp).clm.	158
☐	L13	l12 and $tope	31

END OF SEARCH HISTORY

of the generation of antibody diversity.

CLAIMS:

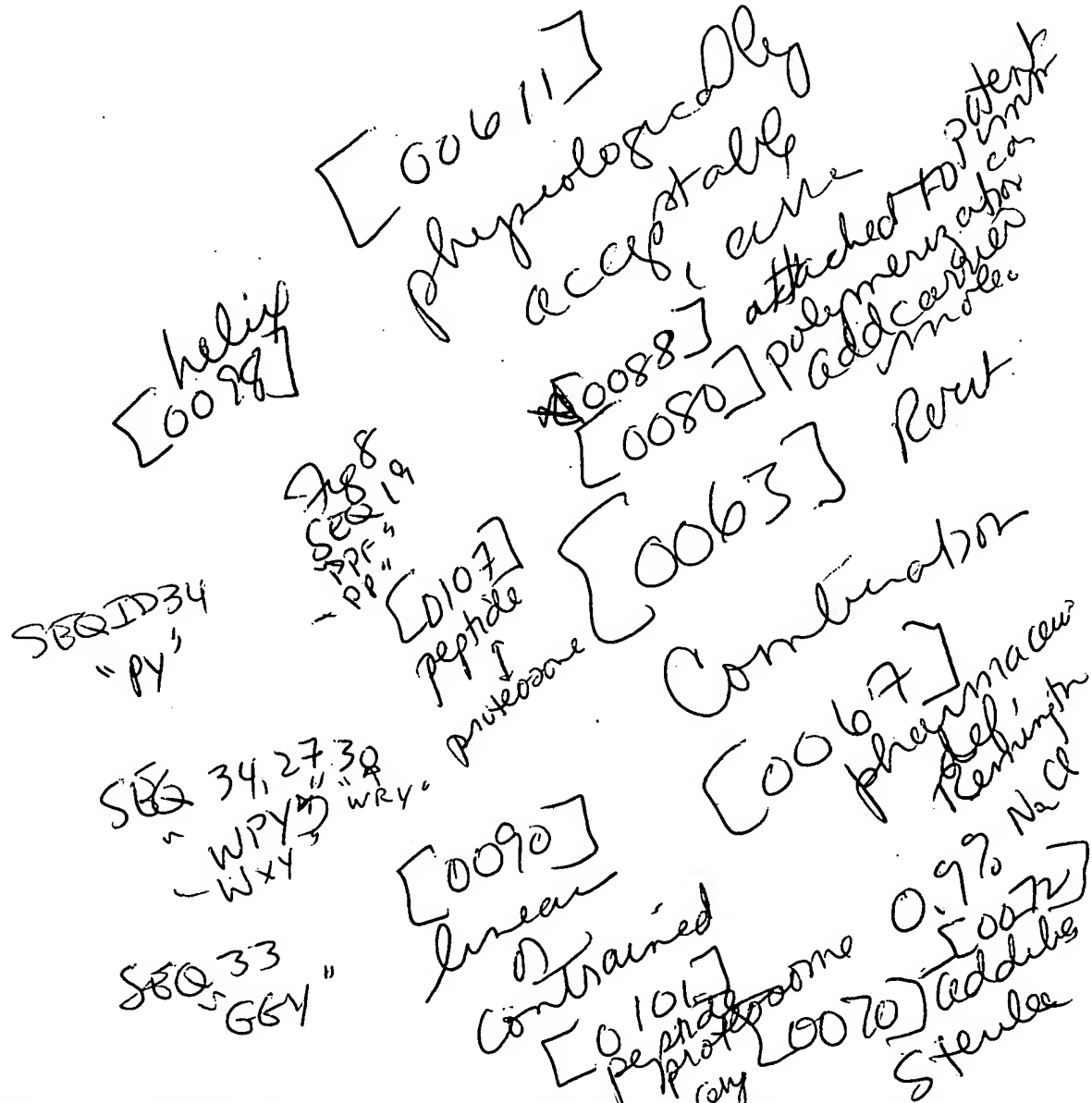
8. A molecular mimetic of a unique epitope of Neisseria meningitidis serogroup B (MenB), wherein said mimetic is comprised of a peptide comprising an amino acid sequence having at least 90% sequence identity to a sequence selected from the group consisting of SEQ ID NOs. 1-7, 9-66, and 67.

Previous Doc Next Doc Go to Doc#

DOCUMENT-IDENTIFIER: US 20030017497 A1
TITLE: Peptide mimotopes of carbohydrate antigens

Detail Description Paragraph:
[0136] We have developed peptides that induce immune responses to carbohydrate structures with in vivo and in vitro functionality. We have found that peptides representative of a W/YXY sequence motif can antigenically and immunologically mimic the meningoccal group C capsular polysaccharide (MCP) of Neisseria meningitidis, Lewis (Le) antigens expressed on tumor cells and mannosyl, lactoseries and sialyl-residues on HIV-1 gp 120. Immunization of mice with peptide fomulations induces IgM and IgG carbohydrate cross-reactive responses. We hypothesize that the utility of peptide mimotopes when formulated into a DNA based vaccine (minigen) could potentially increase the breath of the immune response, redirecting the response to include the induction of Th1 mediated mechanisms associated with the clearance of both pathogens and tumor cells alike.

Previous Doc Next Doc Go to Doc#



UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,051,237

DATED : April 18, 2000

INVENTOR(S) : Yvonne Paterson

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

At Col. 6, Line 16, please delete "pica" and insert therefor --plcA--

Signed and Sealed this

Twenty-seventh Day of March, 2001

Attest:

Nicholas P. Godici

NICHOLAS P. GODICI

Attesting Officer

Acting Director of the United States Patent and Trademark Office

DOCUMENT-IDENTIFIER: US 5599791 A
TITLE: Amides of antibiotic GE 2270 factors

Brief Summary Text (48):
D) The main FAB-MS peak of antibiotic GE 2270 factor C.sub.2a is 1306 daltons. This corresponds most likely to the lowest isotope of the protonated molecular ion. The analysis was performed on a Kratos MS-50 double focusing mass spectrometer, using 8 kV accelerating voltage and a saddle field atom gun with Xe gas (2.times.10.sup.-5 torr pressure indicated on the source ion gauge) at 6 kV voltage and 1 mA current. The antibiotic for the FAB-MS analysis was mixed with a thioglycerol matrix containing 0.1M acetic acid.

CLAIMS:

4. A compound as claimed in claim 1 wherein R is methoxymethyl, R.sub.1 and R.sub.4 represent a methyl group and Y is an amino moiety which is derived from a natural amino acid selected from the group consisting of glycine, ornithine, serine, aspartic acid, tyrosine, leucine, phenylalanine, methionine, proline, threonine, and lysine, or a synthetic dipeptide selected from the group consisting of glycyllysine, serylproline, glycylprolinamide, tyrosylprolinamide, threonylprolinamide, and leucylprolinamide.

8. A compound as claimed in claim 7 wherein Y is an amino moiety which is derived from a natural amino acid selected from the group consisting of glycine, ornithine, serine, aspartic acid, tyrosine, leucine, phenylalanine, methionine, proline, threonine, and lysine, or a synthetic dipeptide selected from the group consisting of glycyllysine, serylproline, glycylprolinamide, tyrosylprolinamide, threonylprolinamide, and leucylprolinamide.

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ile 155:MEDLINE(R) 1950-2006/Sep 27
       (c) format only 2006 Dialog

      Set  Items  Description
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Ref   Items  Index-term
E1       43  ANTIIDIOTYPES
E2      536  ANTIIDIOTYPIC
E3        0 *ANTIIDIOTYPIC ANTIBODIES
E4        3  ANTIIDIOTYPICAL
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E6        1  ANTIIDIOTYPOVE
E7        1  ANTIIDOTYPIC
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E9        2  ANTIIFLAMATORIA
E10       1  ANTIIFLAMMATORI
E11      10  ANTIIFLAMMATORY
E12       1  ANTIIFLAMMTORY

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               2  ANTIIDS
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S2         249   E3-E24
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           44726  MENINGIT?
      S5       3  S4 AND (NEISSER? OR MENINGIT?)
? t s5/9/all

 5/9/1
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

20229362   PMID: 16390937
    Antiidiotypic DNA vaccination induces serum bactericidal activity and
protection against group B meningococci.
  Beninati Concetta; Midiri Angelina; Mancuso Giuseppe; Biondo Carmelo;
Arigo Milena; Gerace Elisabetta; Papasergi Salvatore; Gambuzza Maria;
Boretti Mauro; Magliani Walter; Conti Stefania; Polonelli Luciano; Teti
Giuseppe
  Dipartimento di Patologia e Microbiologia Sperimentale, Universita degli
Studi di Messina, I-98125 Messina, Italy.
  Journal of experimental medicine (United States)  Jan 23 2006,  203  (1)
  p111-8,  ISSN 0022-1007--Print  Journal Code: 2985109R
  Publishing Model Print-Electronic
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed
  Subfile:  INDEX MEDICUS
  No vaccine is available for preventing infections by serogroup B
Neisseria meningitidis (MenB), which accounts for a major portion of
meningococcal cases in developed countries, because of the poor
immunogenicity of the capsular polysaccharide (CP) even after protein
conjugation. We have previously induced anticapsular antibodies by
immunization with a single chain variable fragment (scFv), which mimics a
protective CP epitope. This surrogate antigen, however, was ineffective at
inducing serum bactericidal activity, an accepted marker of protection in
humans. Serum bactericidal activity was consistently achieved by immunizing
mice with the scFv-encoding gene. Immunization with vectors without a
secretory signal sequence before the scFv resulted in markedly higher
bactericidal activity relative to those with such a sequence. The induced
antibodies were capsule specific, as shown by complete inhibition of
bactericidal activity by purified MenB CP and by resistance to killing of
MenA or MenC. Moreover, these antibodies were predominantly of the IgG2a
isotype, reflecting a T helper type 1 response. Administration of sera from
scFv gene-vaccinated animals protected infant rats against MenB bacteremia.
These data illustrate the potential of vaccination with genes encoding
capsular mimics in providing protection against MenB and other encapsulated
```

bacteria.
Descriptors: *Bacterial Vaccines; *Meningococcal Infections--prevention and control--PC; * **Neisseria meningitidis** , Serogroup B--immunology--IM; *Vaccines, DNA; Animals; Animals, Newborn; Antibodies, Bacterial --immunology--IM; Blood Bactericidal Activity; COS Cells; Cercopithecus aethiops; Immunoglobulin Variable Region--immunology--IM; Meningococcal Infections--immunology--IM; Mice; Mice, Inbred BALB C; **Neisseria meningitidis** , Serogroup B--pathogenicity--PY; Rats; Rats, Wistar
CAS Registry No.: 0 (Antibodies, Bacterial); 0 (Bacterial Vaccines); 0 (Immunoglobulin Variable Region); 0 (Vaccines, DNA)
Record Date Created: 20060124
Record Date Completed: 20060329
Date of Electronic Publication: 20060103

5/9/2

DIALOG(R)File 155:MEDLINE(R)

10155561 PMID: 8080172
Antiidiotype **antibodies as surrogates for polysaccharide vaccines.**
Westerink M A; Campagnari A A; Giardina P; Apicella M A
Medical College of Ohio, Toledo 43699-0008.
Annals of the New York Academy of Sciences (UNITED STATES) Aug 15 1994, 730 p209-16, ISSN 0077-8923--Print Journal Code: 7506858
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS
In past studies we demonstrated that monoclonal antibody 6F9 is a surrogate image of the meningococcal C capsular polysaccharide. These studies indicated that immunization with this anti-id resulted in a T-dependent antibody response. In the studies reported in this paper, we show that the response which is elicited is protective. Using a model of meningococcal infection in BALB/c mice in which the animals are rendered susceptible with iron dextran, we studied the ability of this anti-id to protect adult mice against challenge. These studies encompassed the ability of 6F9 to prime neonatal mice and provide them with protection to later challenge. Adult BALB/c mice immunized with 6F9 had a 100% survival and a significantly reduced level of bacteremia at 24 hours. Neonatal mice primed within 24 hours of birth and immunized at 4 weeks of age with 6F9 had a 100% survival and cleared their bacteremia by 8 hours. Neonatal mice primed with 6F9 and challenged at 5 weeks had a 90% survival. These data indicate that anti-id 6F9 is a surrogate antigen for the meningococcal C polysaccharide and is capable of inducing protective immunity in immunologically mature as well as immature animals.
Descriptors: *Antibodies, Anti-Idiotypic--immunology--IM; *Antibodies, Bacterial--immunology--IM; *Bacterial Capsules--immunology--IM; *Bacterial Vaccines--immunology--IM; * **Neisseria meningitidis** --immunology--IM; Animals; Animals, Newborn; Antigens, Bacterial--immunology--IM; Immunologic Memory; Mice; Mice, Inbred BALB C
CAS Registry No.: 0 (Antibodies, Anti-Idiotypic); 0 (Antibodies, Bacterial); 0 (Antigens, Bacterial); 0 (Bacterial Capsules); 0 (Bacterial Vaccines)
Record Date Created: 19941006
Record Date Completed: 19941006

5/9/3

07020957 PMID: 2940174

Effects of antigen and internal environment on anti-phosphorylcholine immune responses of autoimmune aged NZB/W F1 mice.

Seoane R; Faro J; Eiras A; Lareo I; Couceiro J; Regueiro B J

Immunology (ENGLAND) Jun 1986, 58 (2) p329-34, ISSN 0019-2805--Print Journal Code: 0374672
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

The idiotypic profile of anti-phosphorylcholine plaque-forming cell responses and their evolution with ageing were studied in (NZB X NZW) F1 mice. Our results showed that the anti-phosphorylcholine plaque-forming cell response induced by phosphorylcholine coupled to keyhole limpet haemocyanin and, paralleling, the T15 idiotype clonal dominance declined with ageing. This loss of immune competence was also observed with another thymus-dependent (phosphorylcholine coupled to egg globulin) as well as thymus-independent (capsular polysaccharide of Streptococcus pneumoniae strain R36a) antigens. In contrast, old mice challenged with an antigenic preparation of **Neisseria meningitidis** showed an immune response not significantly different from that elicited by the same antigen in young mice. The hapten-augmentable plaque-forming cells were assayed to determine whether a putative auto- **antiidiotypic** regulation underlies this loss of immune competence. Only minimal numbers and non-significant differences between young and old mice immunized with any antigen could be detected. Further studies using an adoptive transfer system demonstrated that cells from aged mice were able to support a normal anti-phosphorylcholine response when transferred into lethally irradiated young recipients. Our results suggest that no permanent cellular defects, but rather internal environment or/and radioresistant suppressor cells, are involved in this loss of immune competence. The role played by these factors and their effect on distinct subpopulations of B cells are discussed.

Tags: Female; Male
Descriptors: *Antibody Formation; *Antigens--immunology--IM; *Choline --analogs and derivatives--AA; *Immunocompetence; *Phosphorylcholine --immunology--IM; Aging; Animals; B-Lymphocytes--immunology--IM; Hemolytic Plaque Technique; Immunization, Passive; Immunoglobulin Idiotypes; Mice; Mice, Inbred Strains; Research Support, Non-U.S. Gov't; Spleen--immunology --IM; T-Lymphocytes, Regulatory--immunology--IM
CAS Registry No.: 0 (Antigens); 0 (Immunoglobulin Idiotypes); 107-73-3 (Phosphorylcholine); 62-49-7 (Choline)
Record Date Created: 19860718
Record Date Completed: 19860718

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PGPUB-DOCUMENT-NUMBER: 20050009748
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050009748 A1

TITLE: Compositions for delivering peptide YY and PYY agonists

PUBLICATION-DATE: January 13, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Dinh, Steve	Ossining	NY	US
Wang, Huaizhen	Chappaqua	NY	US
Gomez-Orellana, M. I.	New Rochelle	NY	US

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	COUNTRY	TYPE CODE
Emisphere Technologies, Inc.	Tarrytown	NY	US	02

APPL-NO: 10/846954 [PALM]
DATE FILED: May 14, 2004

RELATED-US-APPL-DATA:
Application is a non-provisional-of-provisional application 60/470905, filed May 14, 2003,
Application is a non-provisional-of-provisional application 60/471114, filed May 15, 2003,
Application is a non-provisional-of-provisional application 60/506702, filed September 25, 2003,
Application is a non-provisional-of-provisional application 60/536697, filed January 14, 2004,

INT-CL-PUBLISHED: [07] A61K 38/17, A61K 31/195

INT-CL-CURRENT:

TYPE	IPC	DATE
CIPS	A61 K 31/185	20060101
CIPS	A61 K 31/195	20060101
CIPS	A61 K 38/17	20060101

US-CL-PUBLISHED: 514/012; 514/563
US-CL-CURRENT: 514/12; 514/563

REPRESENTATIVE-FIGURES: 1

ABSTRACT:

The present invention provides a composition (e.g., a pharmaceutical composition) comprising at least one delivery agent compound and at least one of peptide YY (PYY) and a PYY agonist. Preferably, the composition includes a therapeutically effective amount of peptide YY or the PYY agonist and the delivery agent compound. The composition of the present invention facilitates the delivery of PYY, a

PYY agonist, or a mixture thereof and increases its bioavailability compared to administration without the delivery agent compound. PPY and PYY agonists possess activity as agents to reduce nutrient availability, including reduction of food intake

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 60/470,905, filed May 14, 2003, U.S. Provisional Patent Application No. 60/471,114, filed May 15, 2003, U.S. Provisional Patent Application No. 60/506,702, filed Sep. 25, 2003, and U.S. Provisional Patent Application No. 60/536,697, filed Jan. 14, 2004, all of which are hereby incorporated by reference.

[0143] To discriminate between these two possibilities, agglutination-inhibition experiments were performed using rabbit anti-type III antibodies, in place of mAb P9D8, to induce agglutination. The rationale behind these studies is that idiotypes unrelated to antigen binding are rarely present in antibodies raised in different species (Westerink et al., 1990).

1TABLE 1

Ability of anti-idiotypic scFv to inhibit
GBS agglutination
by type III-specific antibodies
Anti-type
III antibody Inhibitor Agglutination

None None -

mAb P9D8 ascites.sup.a None +
mAb P9D8 ascites Type III CHO (5
.mu.g/ml) -
mAb P9D8 ascites Group CHO (25 .mu.g/ml) +
mAb
P9D8 ascites C10 scFv (240 .mu.g/ml) -
mAb P9D8 ascites C10 scFv
(120 .mu.g/ml) -
mAb P9D8 ascites C10 scFv (60 .mu.g/ml) -

mAb P9D8 ascites C10 scFv (30 .mu.g/ml) -
mAb P9D8 ascites C10
scFv (15 .mu.g/ml) -
mAb P9D8 ascites C10 scFv (7.5 .mu.g/ml) +

mAb P9D8 ascites H6 scFv (240 .mu.g/ml) +
Absorbed rabbit
serum.sup.b None +
Absorbed rabbit serum Type III CHO (5 .mu.g/ml)
-
Absorbed rabbit serum Group CHO (25 .mu.g/ml) +
Absorbed
rabbit serum C10 scFv (240 .mu.g/ml) -
Absorbed rabbit serum C10
scFv (120 .mu.g/ml) -
Absorbed rabbit serum C10 scFv (60 .mu.g/ml)
-
Absorbed rabbit serum C10 scFv (30 .mu.g/ml) +
Absorbed
rabbit serum H6 scFv (240 .mu.g/ml) +

.sup.aUsed at a
final dilution of 1:125,000
.sup.bUsed at a final dilution of
1:500

Entry 4 of 6 File: USPT Jan 13, 2004

US-PAT-NO: 6676938
DOCUMENT-IDENTIFIER: US 6676938 B1

TITLE: Vaccine formulations comprising antiidiotypic antibodies which immunologically mimic group B streptococcal carbohydrates

DATE-ISSUED: January 13, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Teti; Giuseppe	Messina			IT
Polonelli; Luciano	Parma			IT

US-CL-CURRENT: 424/137.1; 424/135.1, 424/150.1, 424/165.1, 530/300, 530/387.3, 530/387.5, 530/388.4

CLAIMS:

What is claimed is:

1. An isolated scFv fragment that is capable of eliciting a type III capsular polysaccharide-specific protective immune response against group B Streptococcus.

2. The scFv fragment of claim 1, wherein the immune response comprises antibodies that bind to the scFv fragment.

3. The scFv fragment according to claim 1, wherein the immune response comprises T-cells that bind to the scFv fragment.

4. The scFv fragment according to claim 1, wherein the structure of the scFv fragment mimics an antigenic determinant of the type III capsular polysaccharide of group B Streptococcus.

5. The scFv fragment according to claim 1, linked to a carrier protein that is effective to promote the delivery of the scFv fragment to the bloodstream of a patient or which promotes an immune response against the scFv fragment.

6. A composition comprising the scFv fragment according to claim 1 in combination with a pharmaceutically-acceptable excipient.

7. The composition according to claim 6, wherein the excipient is suitable for oral, subcutaneous, intramuscular, topical or intravenous administration.

8. The composition according to claim 6 additionally comprising an adjuvant.

9. The composition according to claim 8, wherein the adjuvant comprises alum.

10. The composition of claim 8, wherein the adjuvant comprises an oil-in-water emulsion.

Detailed Description Text (23):
Synthesis and Biological Activity of a Vaccine Against Neisseria meningitidis Serogroup B

Other Reference Publication (1):
Apicella, The Journal of Infectious Diseases 140(1): 62-72 (1979), "Lipopolysaccharide-Derived Serotype Polysaccharides from Neisseria Meningitidis Group B".

Other Reference Publication (3):
Bundle, The Journal of Biological Chemistry 249(15): 4797-4801 (1974), "Studies on the Group-Specific Polysaccharide of Neisseria Meningitidis Serogroup X and an Improved Procedure for its Isolation".

Other Reference Publication (7):
Jennings et al., The Pathogenic Neisseriae, Proceedings of the Fourth International Symposium, Asilomar, California, Oct. 21-25, 1984, pp. 628-632: "Enhancement of the Immune Response to the Group B Polysaccharide of Neisseria Meningitidis by Means of Its Chemical Modification".

Other Reference Publication (8):
Jennings et al., The Journal of Immunology 134(4): 2651-2657 (1985), "Determinant Specificities of the Groups B and C Polysaccharides of Neisseria Meningitidis".

Other Reference Publication (10):
Jennings et al., The Journal of Immunology 142(10): 3585-3591 (1989), "Unique Intermolecular Bactericidal Epitope Involving the Homosialopolysaccharide Capsule on the Cell Surface of Group B Neisseria Meningitidis and Escherichia ColiK1".

Other Reference Publication (11):
Jennings et al., J. Exp. Med. 165: 1207-1211 (1987): "N-Propionylated Group B Meningococcal Polysaccharide Mimics a Unique Epitope on Group B Neisseria Meningitidis".

Other Reference Publication (14):
Lifely et al., Carbohydrate Research 134: 229-243 (1984), "Rate, Mechanism and Immunochemical Studies of Lactonisation in Serogroup B and C Polysaccharides of Neisseria Meningitidis".

Other Reference Publication (15):
Lifely et al., Carbohydrate Research 156: 123-135 (1986), "Analysis of the Chain Length of Oligomers and Polymers of Sialic Acid Isolated From Neisseria Meningitidis Group B and C and Escherichia ColiK1 and K92".

Other Reference Publication (16):
Marburg et al., J. Am. Chem. Soc. 108: 5282-5287 (1986), "Biomolecular Chemistry of Macromolecules: Synthesis of Bacterial Polysaccharide Conjugates with Neisseria Meningitidis Membrane Protein".

CLAIMS:

3. The immune composition according to claim 2, wherein the bacterium is Neisseria meningitidis.

11. The immune composition of claim 1, wherein the immune composition comprises at least one antibody selected from the group consisting of monoclonal antibodies and antiidiotype antibodies.

First Hit Previous Doc Next Doc Go to Doc#

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L6: Entry 2 of 6 File: PGPB May 27, 2004

DOCUMENT-IDENTIFIER: US 20040101536 A1
TITLE: Vaccine formulations comprising antiidiotypic antibodies which immunologically mimic group B streptococcal carbohydrates

Summary of Invention Paragraph:
[0007] An alternative strategy to obtain effective and boostable antibody responses against carbohydrate antigens involves the development of protein molecules mimicking the conformation of relevant carbohydrate epitopes. The advantage of this approach is that, by their chemical nature, proteins have an intrinsic ability to stimulate T cell help in an antigen-specific way. This strategy resulted in the development of a monoclonal antiidiotypic antibody (mAb) coupled to a carrier protein that was successfully used as a surrogate vaccine to immunoprotect BALB/c mice against lethal Streptococcus pneumoniae infection (McNamara et al., 1984). Monoclonal antibodies mimicking the K13 Escherichia coli (Stein et al., 1984) and the group C Neisseria meningitidis (Westerink et al., 1988) capsular antigens have also been described.

Detail Description Paragraph:
[0195] Westerink, M. A., Campagnari, A. A., Wirth, M. A., & Apicella, M. A. Development and characterisation of an anti-idiotype antibody to the capsular polysaccharide of Neisseria meningitidis serogroup C. Infect. Immun. 56,1120-1127 (1988).

Previous Doc Next Doc Go to Doc#

Summary of Invention Paragraph:
[0011] Peptides mimicking polysaccharides have been reported. For instance, mimotopes of meningococcal group B capsular polysaccharide (Moe et al. 1999. FEMS Immunology and Medical Microbiology 26: 209-226) and meningococcal group C capsular polysaccharide (Westerink et al. 1995 Proc. Natl. Acad. Sci. USA 92: 4021-4025) have been identified. Furthermore, WO 00/25814 discloses several serogroup B LOS L3,7,9 heptapeptide mimotopes.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 01/11409

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K7/04 A61K39/095 G01N33/68 C12N15/11 C12N5/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
CHEM ABS Data, WPI Data, PAJ, EPO-Internal, BIOSIS, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 25814 A (CHARALAMBOUS BAMBOS MICHAEL ;FEAVERS IAN MICHAEL (GB); UNIV LONDON) 11 May 2000 (2000-05-11) cited in the application page 2 -page 7; examples 1,2	1-10, 12-32, 40-45
X	CHARALAMBOUS BAMBOS M ET AL: "Peptide mimics elicit antibody responses against the outer-membrane lipooligosaccharide of group B Neisseria meningitidis." FEMS MICROBIOLOGY LETTERS, vol. 191, no. 1, 1 October 2000 (2000-10-01), pages 45-50, XP002212284 ISSN: 0378-1097 the whole document	1-10, 12-32, 40-45

-/-

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
4 December 2002	10/01/03

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Renggli, J

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 01/11409

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PARTIDOS C D: "Peptide mimotopes as candidate vaccines." CURRENT OPINION IN MOLECULAR THERAPEUTICS. ENGLAND FEB 2000, vol. 2, no. 1, February 2000 (2000-02), pages 74-79, XP001097969 ISSN: 1464-8431 page 76, right-hand column, paragraph 2 ---	1-10, 12-32, 40-45
X	US 5 994 083 A (FELICI FRANCO ET AL) 30 November 1999 (1999-11-30) the whole document -----	45

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 01/11409

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0025814 A	11-05-2000	EP 1124574 A2	22-08-2001
		WO 0025814 A2	11-05-2000
		JP 2002528517 T	03-09-2002
US 5994083 A	30-11-1999	IT 1270939 B	26-05-1997
		AT 170558 T	15-09-1998
		AU 685121 B2	15-01-1998
		AU 6806994 A	12-12-1994
		BR 9406595 A	02-01-1996
		CA 2160486 A1	24-11-1994
		CN 1122613 A ,B	15-05-1996
		DE 69413024 D1	08-10-1998
		DE 69413024 T2	04-02-1999
		DK 698091 T3	07-06-1999
		EP 0698091 A1	28-02-1996
		ES 2120046 T3	16-10-1998
		HK 1011710 A1	31-03-2000
		WO 9426886 A2	24-11-1994
		JP 2813468 B2	22-10-1998
		JP 8506493 T	16-07-1996
		RU 2136697 C1	10-09-1999

PALM Intranet

Application Number [ ] Submit

IDS Flag Clearance for Application 10398104

IDS Information

Content	Mailroom Date	Entry Number	IDS Review	Last Modified	Reviewer
M844	2003-04-01	14	Y ☑	2006-09-27 13:15:49.0	gportner
Update					

J Infect Dis. 1996 Dec;174(6):1238-48.

Links

Experimental immunization with a monoclonal anti-idiotope antibody that mimics the Neisseria gonorrhoeae lipooligosaccharide epitope 2C7.

Gulati S, **McQuillen DP**, **Sharon J**, **Rice PA**.

Department of Medicine, Boston Medical Center, Massachusetts 02118, USA.

An anti-idiotope monoclonal antibody (MAb), called CA1 (Ab2), was produced in mice against MAb 2C7, which recognizes a widely in vivo-expressed gonococcal lipooligosaccharide (LOS) epitope. Mice immunized with MAb CA1 initially had a 2.5-fold increase in IgG (12-fold after a booster) but no increase in IgM anti-LOS (Ab1') antibody. Control mice immunized with LOS had a 4.5-fold rise in IgG and 4-fold rise in IgM anti-LOS antibody. In rabbits, MAb CA1 elicited a 9-fold rise in IgG and a 3.3-fold rise in IgM anti-LOS (Ab1') antibody. Ab1' antibody bactericidal activity was 1-2 logs greater than that produced by immunization with LOS. Ab1' mediated complete human polymorphonuclear leukocyte phagocytosis of 2C7 epitope-positive (but not 2C7 epitope-negative) gonococci. MAb CA1 acts as a molecular surrogate (Ab2beta) for the nominal LOS antigen and may form the basis for vaccine candidates for human immunization against Neisseria gonorrhoeae.

PMID: 8940214 [PubMed - indexed for MEDLINE]

1: Hybridoma. 1999 Apr;18(2):121-9.

Links

Human immune response to a peptide mimic of Neisseria meningitidis serogroup C in hu-PBMC-SCID mice.

Hutchins WA, **Kieber-Emmons T**, **Carlone GM**, **Westerink MA**.

Department of Medicine, Medical College of Ohio, Toledo 43699, USA.

An anti-idiotype-based peptide mimic vaccine for Neisseria meningitidis serogroup C polysaccharide (MCPS) has been developed and shown to induce a response in mice that is specific, functional, and T-dependent. In this study, the immunogenicity of the MCPS peptide mimic vaccine preparation, as a potential vaccine for use in humans, is shown using the hu-PBMC-SCID mouse model. The human antibody response to the MCPS peptide mimic vaccine is specific and functional as shown by inhibition enzyme-linked immunoadsorbent assay (ELISA) and bactericidal assay. These data support the usefulness of the peptide mimic vaccine strategy for humans.

PMID: 10380011 [PubMed - indexed for MEDLINE]

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : G01N 33/53, 33/536, 3/543	A1	(11) International Publication Number: WO 99/40433
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(30) Priority Data:
60/073,690 4 February 1998 (04.02.98) US

(71) Applicant *(for all designated States except US)*: THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA [US/US]; Suite 300, 3700 Market Street, Philadelphia, PA 19104 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: KIEBER-EMMONS, Thomas [US/US]; 3231 Saw Mill Road, Newtown Square, PA 19073 (US).

(74) Agents: MACKIEWICZ, John, J. et al.; Woodcock Washburn Kurtz Mackiewicz & Norris LLP, 46th floor, One Liberty Place, Philadelphia, PA 19103 (US).

(81) Designated States: AU, CA, JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

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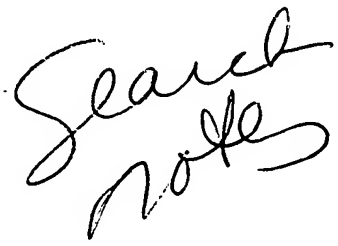

(54) Title: PEPTIDE MIMOTOPES OF CARBOHYDRATE ANTIGENS

(57) Abstract

Methods of preparing a peptide and antigenic antibodies which mimic an antigenic carboyhdrate are disclosed. The method comprises the steps of identifying a peptide sequence which is immunogenically cross reactive an antigenic carbohydrate and synthesizing a peptide or recombinant antibody which comprises the peptide sequence. Methods of generating an immune response against a pathogen or tumor cell in an individual using such peptides, recombinant antibodies comprising such peptide, or DNA vaccines live attenuated vaccines, or recombinant vaccines that encode such peptides are disclosed. Methods of enhancing binding of anti-antigenic carbohydrate antibodies to the antigenic carbohydrate in an individual are disclosed. The methods comprise administering to an individual anti-antigenic carbohydrate antibodies and a peptide which mimics the antigenic carbohydrate. Methods of inhibiting binding of a ligand to a receptor which is an antigenic carbohydrate are disclosed. The methods comprise administering to an individual a peptide which mimics an antigenic carbohydrate. Methods of identifying peptide sequences which can induce an immune response against two or more different pathogens are disclosed. Novel compositions are disclosed.

Table 4. Summary of Complement Dependent Cytotoxicity Results

Tumor	C1	P2	P1	P3	G1	G2	B1	LeY-PAA	ME361	BR55-2
SKMEl-28	3	13	10	32	75	87	10	4	53 (50μg)	3 (100μg)
SKBR3	6	80	90	86	10	13	90	20	10 (100μg)	80(100μg)
MCF-7	3	29	66	56	20	15	70	26	5 (50μg)	75(100μg)
WM793	5	9	9	28	90	90	10	2	63 (30μg)	1 (100μg)
OVAR-3	5	84	89	86	9	11	85	25	6(50μg)	80(100μg)

Values are averaged percent cytotoxicity. Final dilutions are 1:15 for sera. Monoclonal antibody ME361 and BR55-2 concentrations are per ml.

Peptides used in these studies .

SEQ ID NO: 37	G1	GVVWRYTAPVHLGDG	ME361 phage screen
SEQ ID NO: 38	G2	LDVVLAWRDGLSGAS	ME361 phage screen
SEQ ID NO: 39	P1	GGIYYPYDIYYPYDIYYPYD	Repeating motif of Con A phage screen
SEQ ID NO: 40	P2	GGIYWRYDIYWRYDIYWRYD	Repeating motif from amylase inhibitor
SEQ ID NO: 41	P3	GGIYYRYDIYYRYDIYYRYD	Repeating motif of anti-Id
SEQ ID NO: 42	P4	GSSFWRYTTYYDPS	FH-6 phage screen
SEQ ID NO: 43	B1	IMILLIFSLLWFGGA	BR55-2 phage screen
SEQ ID NO: 44	C1	GDTRYIPALQHGDKK	Irrelevant Control

in analyzing closely related interactive sites of proteins in general and of antibodies in particular. Peptide mimotopes of carbohydrate antigens that can be rendered immunogenic can provide an alternative immunogen for carbohydrate antigens that are difficult to isolate or synthesize. In addition, peptide mimotopes provide an alternative to identifying epitopes that are otherwise not defined chemically as those associated with some complex carbohydrate determinants.

Peptide libraries provide an almost infinite source of molecular shapes, amongst which one would expect to find mimics of any given antigen. Screening of random peptide libraries with monoclonal libraries has selected specific peptides. Such peptides will reflect the conformation of the antigen binding site and may provide molecular mimotopes of particular epitopes. Although peptide libraries have been used to identify mimotopes for a few saccharides, it was not certain that peptide mimotopes could be identified that would bind well enough to inhibit the binding of antibodies to carbohydrate antigens or induce immune responses that are protective in nature.

Peptide mimotopes for carbohydrates have been defined containing a two aromatic amino acid repeat motif W/YXY found to Con A (YPY), in peptides that mimic the Lewis Y antigen (WLY), in peptides that bind to antibodies to the meningococcal group C capsular polysaccharide (YRY), and in antibodies that bind to Crytococcous epitopes. These observations argue that a particular peptide structure is required for polysaccharide mimicry. Antibody heavy chain complementarity regions constitute a natural constrained loop peptide library that are rich in aromatic amino acids, especially tyrosine. Binding site specific anti-anti-idiotypic antibodies can serve as mimotopes for polysaccharide antigens. In this context , the binding site of an anti-idiotypic antibody could be looked upon as a way of presenting peptides so that they will mimic a particular conformation of a non-protein antigen. A more precise understanding of the binding of peptides and saccharides at the molecular level is required in order to determine whether the occurrence of motifs like W/YXY in mimotopes of saccharide structures is due to molecular mimicry or simply reflects an advantage provided by aromatic rings for interactions between proteins. In addition to the role that peptide mimotopes can play in exploring the fine specificity of antibodies, they may mimic polysaccharides as antigen and potentially elicit an anti-oligosaccharide response. Not all peptides that have been isolated

[0036] As described above, the large number of peptide mimotopes identified by the phage display technique allows the identification of patterns which define an epitope (or part of an epitope) of a mimotope of L3,7,9 LOS. Accordingly a further aspect of the invention is peptide mimotopes of L3,7,9 LOS comprising the amino acid sequence (either linear or cyclised): WY; PP; AP; PY; PPY; PPF; PPW; APP; WYS; WYT; LWY; GGY; GPY; PPYD (a preferred motif); PPFD; FDPP; GGYL; PPWD; SLWY; PXWY; WYXXP; YXY; PWST; EKKXF or WXY (where each X is the same or different and is an amino acid, preferably a naturally-occurring amino acid).

SEQ ID 19 WO99

WO 99/40433

PY
PYD

WXY
YXY

Reduced Cov (as) Comp

DOCUMENT-IDENTIFIER: US 20060035284 A1
TITLE: Methods for isolating molecular mimetics of unique Neisseria meningitidis serogroup B epitopes

Brief Summary Text:
[0006] MenB PS derivatives have been prepared in an attempt to circumvent the poor immunogenicity of MenB PS. For example, C.sub.3-C.sub.8 N-acyl-substituted MenB PS derivatives have been described. See, EP Publication No. 504,202 B, to Jennings et al. Similarly, U.S. Pat. No. 4,727,136 to Jennings et al. describes an N-propionylated MenB PS molecule, termed "NPr-MenB PS" herein. Mice immunized with NPr-MenB PS glycoconjugates were reported to elicit high titers of IgG antibodies. Jennings et al. (1986) J. Immunol. 137:1708. In rabbits, two distinct populations of antibodies, purportedly associated with two different epitopes, one shared by native MenB PS and one unshared, were produced using the derivative. Bactericidal activity was found in the antibody population that did not cross react with MenB PS. Jennings et al. (1987) J. Exp. Med. 165:1207. The identity of the bacterial surface epitope(s) reacting with the protective antibodies elicited by this conjugate remains unknown.

Brief Summary Text:
[0014] Still further embodiments of the subject invention are related to methods for isolating molecular mimetics of unique epitopes of MenB PS and molecular mimetics identified using the methods. The methods comprise: [0015] (a) providing a population of molecules including a putative molecular mimetic of a unique epitope of MenB PS; [0016] (b) contacting the population of molecules with the antibodies described above under conditions that allow immunological binding between the antibody and the molecular mimetic, if present, to provide a complex; and [0017] (c) separating the complexes from non-bound molecules.

Brief Summary Text:
[0018] In another embodiment, the subject invention is directed to a vaccine composition comprising a unique epitope of MenB in combination with a pharmaceutically acceptable excipient.

Brief Summary Text:
[0019] In yet another embodiment, the invention is directed to a vaccine composition comprising a molecular mimetic of a unique epitope of MenB in combination with a pharmaceutically acceptable excipient.

Brief Summary Text:
[0020] In still a further embodiment, the invention is directed to a vaccine composition comprising an anti-idiotypic antibody molecular mimetic of a unique epitope of MenB in combination with a pharmaceutically acceptable excipient.

Description of Disclosure:
[0042] "Molecular mimetics" of MenB PS, or derivatives of MenB PS are molecules that functionally mimic at least one "unique" epitope expressed on a MenB bacteria. A "unique epitope" is an epitope capable of eliciting the formation of functionally active (e.g., opsonic and/or complement-mediated bactericidal) anti-MenB antibodies that either are not cross-reactive with polysialic acid in host tissue and hence lack autoimmune activity, or are minimally cross-reactive. Such molecular mimetics are useful in vaccine compositions and in eliciting antibodies for diagnostic or therapeutic applications, as described further below. Molecular mimetics include, but are not limited to, small organic compounds; nucleic acids and nucleic acid derivatives; saccharides or oligosaccharides; peptide mimetics including peptides, proteins, and derivatives thereof, such as peptides containing non-peptide organic moieties,

synthetic peptides which may or may not contain amino acids and/or peptide bonds, but retain the structural and functional features of a peptide ligand, and peptoids and oligopeptoids which are molecules comprising N-substituted glycine, such as those described by Simon et al. (1992) Proc. Natl. Acad. Sci. USA 89:9367; and antibodies, including anti-idiotype antibodies. Methods for the identification and production of molecular mimetics are described more fully below.

Description of Disclosure:
[0046] By "epitope" is meant a site on an antigen to which specific B cells and T cells respond. The term is also used interchangeably with "antigenic determinant" or "antigenic determinant site." A peptide epitope can comprise 3 or more amino acids in a spatial conformation unique to the epitope. Generally, an epitope consists of at least 5 such amino acids and, more usually, consists of at least 8-10 such amino acids. Methods of determining spatial conformation of amino acids are known in the art and include, for example, x-ray crystallography and 2-dimensional nuclear magnetic resonance spectroscopy. Furthermore, the identification of epitopes in a given protein is readily accomplished using techniques well known in the art. See, e.g., Geysen et al. (1984) Proc. Natl. Acad. Sci. USA 81:3998 (general method of rapidly synthesizing peptides to determine the location of immunogenic epitopes in a given antigen); U.S. Pat. No. 4,708,871 (procedures for identifying and chemically synthesizing epitopes of antigens); and Geysen et al. (1986) Molecular Immunology 23:709 (technique for identifying peptides with high affinity for a given antibody). Antibodies that recognize the same epitope can be identified in a simple immunoassay showing the ability of one antibody to block the binding of another antibody to a target antigen.

Description of Disclosure:
[0047] A "unique MenB epitope" is defined herein as an epitope present on a MenB bacterium, wherein antibodies directed toward the epitope are capable of binding specifically to MenB and not cross reacting, or minimally cross reacting, with sialic acid residues present on the surface of host tissue. Immunogens containing or mimicking one or more "unique MenB epitopes" are thus useful in vaccines for prevention of MenB disease, and will not elicit an autoimmune response, or pose minimal risk of eliciting an autoimmune response.

Description of Disclosure:
[0049] An antibody specific for a "unique" MenB epitope "lacks autoimmune activity," and/or is "not autoreactive" when the subject antibody does not exhibit cross-reactive immunological binding properties with polysialic acid in host tissue as determined using the binding assays described herein.

Description of Disclosure:
[0050] An antibody specific for a "unique" MenB epitope is "not autoreactive" when the subject antibody requires approximately ten times greater antibody concentration to exhibit binding to polysialic acid in host tissues, compared to a known cross-reactive auto antibody considered positive in the binding assays described herein. (For example, compare binding of SEAM-12 to binding of SEAM-35 in FIG. 6). Thus, the term encompasses those antibodies that are not autoreactive or minimally autoreactive in the binding assays described herein.

Description of Disclosure:
[0096] Anti-idiotypic antibodies can also be produced using the anti-MenB antibodies of the present invention for use as molecular mimetics of unique epitopes of MenB. For a review of anti-idiotype antibodies, see, e.g., Kieber-Emmons et al. (1986) Int. Rev. Immunol. 1:1. In this regard, the pocket or cleft formed by the heavy and light chains of an antibody is often intimately involved in antigen binding. This region, called the paratope, is an "internal image" of the antigen surface bound by the antibody. An antibody directed against the paratope is one of several potential anti-idiotypic antibodies and can be a mimetic of the antigen. Randomized peptide loops of the heavy and light chains occur naturally as part

of the generation of antibody diversity.

CLAIMS:

8. A molecular mimetic of a unique epitope of Neisseria meningitidis serogroup B (MenB), wherein said mimetic is comprised of a peptide comprising an amino acid sequence having at least 90% sequence identity to a sequence selected from the group consisting of SEQ ID NOs. 1-7, 9-66, and 67.

Previous Doc Next Doc Go to Doc#

DOCUMENT-IDENTIFIER: US 20060035284 A1
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